REMARKS

Rejection under 35 USC 103(a) in view of Cullinan et al. and Devogelaer et al.

Claims 11-14, 20, 30, 3-36, 40, 42-47, and 51-54 are rejected as allegedly being obvious in view of Cullinan et al. (US 5,593,987) in combination with the article by Devogelaer et al. This rejection is respectfully traversed.

Cullinan et al. disclose a method of inhibiting breast disorders comprising administering a compound from a select group of 2-phenyl-3-aroylbenzothiophenes. See, e.g., column 2, lines 14-17. This group is defined by formula I (see column 1, line 34-column 2, line 9) which includes the compound Raloxifiene (see column 2, lines 30-34). As noted in the rejection, Cullinan et al. do not teach or suggest using Raloxifene, or any other compound, to ameliorate LHRH analogue-induced reduction in bone density in a patient. In fact, Cullinan et al. make no mention of bone density, nor any mention of LHRH analogues inducing a reduction in bone density.

At column 2, lines 34-43, Cullinan et al. disclose the mixed agonist-antagonist activity of Raloxifene with respect to the estrogen receptor. It is disclosed that Raloxifene blocks the action of estrogen in some cells. However, in other cells, "Raloxifene activates the same genes as estrogen does and displays the same pharmacology, e.g., osteoporosis, hyperlipidemia."

Devogelaer et al. disclose the results of a study in which the LHRH analogue buserelin was administered to patients with endometriosis for 6 months. Bone loss for the lumbar spine and distal radius was observed. Devogelaer et al. also disclose that prior reports indicate that trabecular bone decreases before menopause, which increases after menopause, which can be "counteracted by the administration of oestrogens."

The rejection argues that it would be obvious to administer Raloxifene at the same time or after administration of LHRH analogues to ameliorate LHRH analogue-induced reduction in bone density. However, neither reference discloses a dosing regime in which both an LHRH analogue and an estrogen, or for that matter, Raloxifene. Thus, neither reference discloses or suggests ameliorating LHRH analogue-induced reduction in bone density by administering one or more LHRH analogues and Raloxifene which are administered sequentially or simultaneously.

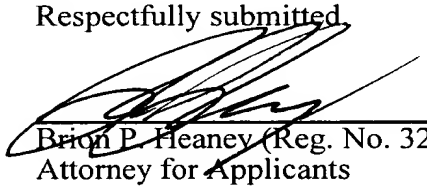
Furthermore, as noted by Cullinan et al., Raloxifene has a complex activity with respect to the estrogen receptor. In light of this, one of ordinary skill in the art would not

merely assume that one could replace estrogen treatment with Raloxifene treatment. Even if both have osteoporosis activity, this does not suggest that both could be used to treat bone loss associated with the administration of LHRH analogues. Moreover, even if the cited prior art references suggested the use of estrogens in combination with LHRH analogues to address LHRH analogue-induced reduction in bone density (which they do not), one of ordinary skill in the art can not simply assume that administering Raloxifene will not adverse affect the activity of the LHRH analogues. Further, since Raloxifene and estrogens clearly have different activities spectrums, one of ordinary skill in the art would have no reasonable expectation of success concerning a method involving administration one or more LHRH analogues and Raloxifene which are administered sequentially or simultaneously.

In view of the above remarks, it is respectfully submitted that Cullinan et al. (US 5,593,987), alone or in combination with the article by Devogelaer et al., fail to render obvious applicants' claimed invention. Withdrawal of the rejection is respectfully requested. In view of the above, allowance of the instant application is respectfully requested.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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